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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/499,875	02/08/2000	Richard Griffey	IBIS-0261	1850

34138 7590 10/16/2003

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EXAMINER
TRAN, MY CHAU T

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 10/16/2003

23

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/499,875	Applicant(s) GRIFFEY ET AL.	
	Examiner My-Chau T. Tran	Art Unit 1639	

-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-32 and 34-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-32 and 34-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Note: The examiner for your application in the PTO has changed. However, the Group and/or Art Unit location of your application in the PTO is remained the same, which is Group Art Unit 1639.

1. The status of the claims is as follows: Claim 33 is canceled by the amendment in Paper No. 16. Claims 1-29 and 47-120 are canceled by the amendment in Paper No. 14.

2. Claims 30-32, and 34-46 are pending.

Maintained Rejections

3. Claims 30-32 and 34-46 are treated on the merit in this Office Action.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Double Patenting

5. Claims 30-32 and 34-46 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 10-19 of U.S. Patent No. 6,329,146 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the presently claimed method is obvious over the method disclosed in the '146 patent.

The present claims are drawn to a method of selecting members of a library of 2-1000,000 compounds (of less than 200 Daltons and having fewer than 4 rotatable bonds) that can form a non-covalent complex with a target RNA molecule comprising: [1] mixing a standard ligand with an excess of target RNA molecule; [2] introducing the mixture into an electrospray mass spectrometer and adjusting the operational parameters so that the relative ion abundance signal of the standard ligand-target RNA molecule complex is between 1% and 30% that of the unbound target molecule; [3] introducing 2-8 compounds from the library into a test mixture of standard ligand-target RNA molecule; [4] identifying members of the groups of compounds that form non-covalent complexes with the target RNA molecule by discerning relative ion abundance signals that arise from complexes formed between the target RNA molecule and members of the groups of compounds and identifying the compounds by their relative molecular masses; and [5] storing and cross-indexing relative abundance and stoichiometry data of complexes in a relational database.

The '146 patent teaches a method for identifying in a combinatorial mixture compounds which bind to a target RNA comprising: [1] providing a complex of RNA target and standard binding compound; [2] combining the complex with a combinatorial mixture of compounds; [3] collecting mass spectral (relative) ion abundance data on the mixture formed in [2] and using (relative) ion abundance data collected for the complex in [1] to afford information that allows the determination of which compounds from the combinatorial mixture bind to the target RNA.

The '146 method clearly requires the selection of a mass spectrometer and collecting ion abundance data for a standard ligand-RNA complex as well as a mixture including the standard ligand-RNA complex plus compounds form a combinatorial mixture. Column 48 of the '146

patent teaches that the target molecule must be in excess over the standard ligand and columns 48-49 teach the use of relational databases for the results of electrospray mass spectroscopy embodiments of the cited method. The referenced method can be used with combinatorial libraries of potential ligands from metal ions to small organic molecules (i.e. less than 200 Daltons and fewer than 4 rotatable bonds) to large molecules including, for example, 20-5000 compounds. The method is exemplified using a library of 216 organic molecules and paromomycin as a standard ligand.

The '146 patent does not specify particular relative signal strengths libraries limited to compounds of various molecular weight ranges or numbers of rotatable bonds. Such optimizations and selections of parameters were well within the abilities of one of ordinary skill in the art at the time the invention was made.

Response to Arguments

6. Applicant's argument(s) directed to the above rejection under the judicially created doctrine of obviousness-type double patenting for claim(s) 30-32 and 34-46 over claims 10-19 of U.S. Patent No. 6,329,146 B1 have been fully considered but they are not persuasive for the following reason(s).

7. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., applicant argues that "[t]he claimed process includes the step of adjusting the mass spectrometer desolvation conditions using standard ligand to provide resolution of a low-strength labile signal" (see specification, page 11, lines 29-33)) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification

are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claim Rejections - 35 USC § 102

8. Claims 30-32 and 34-46 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent No. 6,329,146 B1 Crooke et al. December 2001.

The present claims are drawn to a method of selecting members of a library of 2-1000,000 compounds (of less than 200 Daltons and having fewer than 4 rotatable bonds) that can form a non-covalent complex with a target RNA molecule comprising: [1] mixing a standard ligand with an excess of target RNA molecule; [2] introducing the mixture into an electrospray mass spectrometer and adjusting the operational parameters so that the relative ion abundance signal of the standard ligand-target RNA molecule complex is between 1% and 30% that of the unbound target molecule; [3] introducing 2-8 compounds from the library into a test mixture of standard ligand-target RNA molecule; [4] identifying members of the groups of compounds that form non-covalent complexes with the target RNA molecule by discerning relative ion abundance signals that arise from complexes formed between the target RNA molecule and members of the groups of compounds and identifying the compounds by their relative molecular masses; and [5] storing and cross-indexing relative abundance and stoichiometry data of complexes in a relational database.

The '146 patent teaches a method for identifying in a combinatorial mixture compounds which bind to a target RNA comprising: [1] providing a complex of RNA target and standard binding compound; [2] combining the complex with a combinatorial mixture of compounds; [3]

collecting mass spectral (relative) ion abundance data on the mixture formed in [2] and using (relative) ion abundance data collected for the complex in [1] to afford information that allows the determination of which compounds from the combinatorial mixture bind to the target RNA.

The '146 method clearly requires the selection of a mass spectrometer and collecting ion abundance data for a standard ligand-RNA complex as well as a mixture including the standard ligand-RNA complex plus compounds form a combinatorial mixture. Column 48 of the '146 patent teaches that the target molecule must be in excess over the standard ligand and columns 48-49 teach the use of relational databases for the results of electrospray mass spectroscopy embodiments of the cited method. The referenced method can be used with combinatorial libraries of potential ligands from metal ions to small organic molecules (i.e. less than 200 Daltons and fewer than 4 rotatable bonds) to large molecules including, for example, 20-5000 compounds. The method is exemplified using a library of 216 organic molecules and paromomycin as a standard ligand.

Response to Arguments

9. Applicant's argument(s) directed to the above rejection under 35 USC 102(e) as being anticipated by US Patent No. 6,329,146 B1 Crooke et al. December 2001 for claims 30-32 and 34-46 was considered but they are not persuasive for the following reasons.

In response to Applicant's argument that Crooke et al. "[d]oes not teach or suggest a method which comprises adjusting the operating performance conditions of the mass spectrometer such that the signal strength of the standard compound bound to the target molecule is from 1% to about 30% of signal strength of unbound target molecule", a claim is anticipated if each element of the claim is found, either expressly described or under principles of inherency,

in a single prior art reference, or that the claimed invention was previously known or embodied in a single prior art device or practice. In this case the limitation of adjusting the operating performance conditions of the mass spectrometer such that the signal strength of the standard compound bound to the target molecule is from 1% to about 30% of signal strength of unbound target molecule, is inherently a routine optimization step in the method of mass spectrometry. Therefore, the method of Crooke et al. anticipates the presently claimed invention.

Conclusion

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 703-305-6999. The examiner is on Increased Flex Schedule and can normally be reached on Monday: 8:00-2:30; Tuesday-Thursday: 7:30-5:00; Friday: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang can be reached on 703-306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123.

mct

October 8, 2003

PADMASHRI PONNALURI
PRIMARY EXAMINER